Complete Summary

GUIDELINE TITLE

Postmenopausal hormone replacement therapy for primary prevention of cardiovascular and cerebrovascular disease. Recommendation statement from the Canadian Task Force on Preventive Health Care.

BIBLIOGRAPHIC SOURCE(S)

Abramson BL. Postmenopausal hormone replacement therapy for primary prevention of cardiovascular and cerebrovascular disease. Recommendation statement from the Canadian Task Force on Preventive Health Care. CMAJ 2004 Apr 27;170(9):1388-9. [35 references] PubMed

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Cardiovascular disease
Cerebrovascular disease

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Prevention

CLINICAL SPECIALTY

Cardiology
Family Practice
Geriatrics
Internal Medicine
Obstetrics and Gynecology
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To systematically review the current evidence and make recommendations for the use of hormone replacement therapy (HRT) for primary prevention of cardiovascular and cerebrovascular disease

TARGET POPULATION

Perimenopausal women without established cardiovascular or cerebrovascular disease

INTERVENTIONS AND PRACTICES CONSIDERED

Hormone replacement therapy (HRT)

1. Combined estrogen and progestin therapy
2. Estrogen-only (for women without an intact uterus)

MAJOR OUTCOMES CONSIDERED

- Cardiac disease outcomes: myocardial infarction incidence or cardiovascular disease mortality
- Cerebrovascular disease outcomes: stroke incidence and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE was searched for all English language articles published from 1966 to February 2001 using the Medical Subject Heading (MeSH) terms: "Estrogen Replacement Therapy" from 1991 forward, in addition "Estrogens – conjugated" and "Estrogens –synthetic" from 1966 to 1990 AND ["cardiovascular diseases", OR "cerebrovascular disorders", OR "myocardial infarction" OR "coronary disease" OR the keyword "mortality" as a text word in the title or abstract]. Scanning the bibliographies of the retrieved articles and review articles identified additional articles. In studies with multiple publications, the version with the longest follow up duration was included in the analysis. Key studies published after the search end date, were also added.

To limit the analysis to studies with the highest methodologic quality, selection criteria were used to limit the analysis to prospective cohort studies with internal controls or randomised controlled trials (RCT) with a minimum follow-up of 5 years. The addition of a recent large RCT published in 2002 has been added to the analysis.

Specific inclusion and exclusion criteria were as follows:

Inclusion Criteria

- The study was either a prospective cohort study with internal controls or a randomised controlled trial investigating the prevention of death, myocardial infarction, or stroke from hormone replacement therapy consisting of either estrogen or estrogen in combination with progestin.
- The duration of the patient follow-up was at least 5 years.
- The majority of patients initially studied were free from established coronary or cerebrovascular disease.
- Human females were studied.

Exclusion Criteria

- Agents such as Selective Estrogen Receptor Modulators (SERMs) were utilized (as these compounds are still under investigation for cardio-protection and have some antiestrogen properties in addition to estrogen like effects).
- There was no documentation of patients lost to follow-up.
- Men were included in the study population and data from the female sub-group could not be separated.
- The study evaluated premenopausal estrogen use.
- The study did not have internal controls or had a solely a case-control design, although prospective cohorts with nested case control analyses were included.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

I: Evidence from well-designed randomized controlled trial(s)

II-1: Evidence from well-designed controlled trial(s) without randomization

II-2 Evidence from well-designed cohort or case–control analytic studies, preferably from more than one centre or research group

II-3: Evidence from comparisons between times or places with or without the intervention; dramatic results from uncontrolled studies could be included here

III: Opinions of respected authorities, based on clinical experience; descriptive studies or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

All eligible studies were systematically reviewed using the methodology of the Canadian Task Force on Preventive Health Care. The Task Force, comprising expert clinicians and methodologists from a variety of medical specialties, uses a standardized evidence-based method for evaluating effectiveness. The strength of evidence was evaluated using the evidence-based methods of the Canadian Task Force on Preventive Health Care.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Evidence for this topic was presented by the lead author(s) and deliberated upon during task force meetings in June and October 1999, May 2002, and February 2003. Expert panelists addressed critical issues, clarified ambiguous concepts and analyzed the synthesis of the evidence. At the end of this process, the specific clinical recommendations proposed by the lead author were discussed, as were issues related to clarification of the recommendations for clinical application and any gaps in evidence. The results of this process are reflected in the description of the decision criteria presented with the specific recommendations. The group and lead author(s) arrived at final decisions on recommendations unanimously.

Subsequent to the meetings, the lead author revised the manuscript accordingly. After final revision, the manuscript was sent by the Task Force to two experts in the field (identified by Task Force members at the meeting). Feedback from these experts was incorporated into a subsequent draft of the manuscript.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendations Grades for Specific Clinical Preventive Actions

A: The Canadian Task Force (CTF) concludes that there is good evidence to recommend the clinical preventive action.

B: The CTF concludes that there is fair evidence to recommend the clinical preventive action.

C: The CTF concludes that the existing evidence is conflicting and does not allow making a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.

D: The CTF concludes that there is fair evidence to recommend against the clinical preventive action.

E: The CTF concludes that there is good evidence to recommend against the clinical preventive action.

I: The CTF concludes that there is insufficient evidence (in quantity and/or quality) to make a recommendation; however, other factors may influence decision-making.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

External Peer Review

After final revision, the manuscript was sent by the Task Force to two experts in the field (identified by Task Force members at the meeting). Feedback from these experts was incorporated into a subsequent draft of the manuscript.

Comparison with Recommendations of Other Groups

Several groups have issued updated recommendations following the release of the Women´s Health Initiative (WHI) study results: The United States Preventive Services Task; The Society of Obstetrics and Gynaecology of Canada (SOGC); The Heart and Stroke Foundation of Canada in collaboration with the Canadian Cardiovascular Society; The American Society of Obstetrics and Gynaecology (ACOG); and The North American Menopause Society.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendation grades [A, B, C, D, E, I] and levels of evidence [I, II-1, II-2, II-3, III] are indicated after the recommendation. Definitions for these grades and levels of evidence are repeated following the recommendation.

Hormone replacement therapy for the primary prevention of cardiac disease and cardiac mortality in perimenopausal women. There is fair evidence to recommend against the use of hormone replacement therapy (HRT) for the primary prevention of myocardial infarction and death from cardiovascular disease in perimenopausal women without established coronary artery disease (CAD). [D recommendation]

For combined estrogen plus progestin therapy:

- Increased risk of non-fatal myocardial infarction (MI) and coronary death (7 more cases/10,000)
- Increased risk of stroke (8 more cases/10,000), venous thromboembolism (18 more cases/10,000).

Overall increased relative risk of 22% of an adverse outcome for cardiovascular disease.

[Supporting Evidence: Cauley et al., 1997; Falkeborn et al., 1992; Falkeborn et al., 1993; Finucane et al., 1993; Folsom et al., 1995; Lafferty & Fiske, 1994; Schairer et al.,1997; Sourander et al., 1998; Sturgeon et al., 1995; Hernandez Avila, Walker, & Jick, 1990; Bush et al., 1987; Criqui et al., 1988; Grodstein et al., 1996; Henderson, Paganini-Hill, & Ross, 1991; Nachtigall et al., 1979; Wilson, Garrison, & Castelli, 1985; Wolf et al., 1991]

To maintain heart health, women should be advised to adopt other effective preventive strategies, such as lifestyle changes that include increased exercise, lower fat diets, smoking cessation, and blood pressure assessment and control.

There is insufficient evidence to make a recommendation on HRT for the primary prevention of stroke and death from cerebrovascular disease (CVD). Since stroke is a major cause of morbidity and mortality in Canadian women, other beneficial preventive measures, such as aggressive treatment of hypertension, should be used rather than HRT.

Definitions:

Recommendations Grades for Specific Clinical Preventive Actions

A: The Canadian Task Force (CTF) concludes that there is good evidence to recommend the clinical preventive action.

B: The CTF concludes that there is fair evidence to recommend the clinical preventive action.

C: The CTF concludes that the existing evidence is conflicting and does not allow making a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.

D: The CTF concludes that there is fair evidence to recommend against the clinical preventive action.

E: The CTF concludes that there is good evidence to recommend against the clinical preventive action.

I: The CTF concludes that there is insufficient evidence (in quantity and/or quality) to make a recommendation; however, other factors may influence decision-making.

Levels of Evidence

I Evidence from well-designed randomized controlled trial(s)

II-1 Evidence from well-designed controlled trial(s) without randomization

II-2 Evidence from well-designed cohort or case–control analytic studies, preferably from more than one centre or research group

II-3 Evidence from comparisons between times or places with or without the intervention; dramatic results from uncontrolled studies could be included here

III Opinions of respected authorities, based on clinical experience; descriptive studies or reports of expert committees

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Maneuver: Hormone replacement therapy for the primary prevention of cardiac disease and cardiac mortality in peri-menopausal women.

Level of Evidence

Seven prospective cohort studies with internal controls, or randomized controlled trials (I, II-2)

Twelve additional prospective cohort studies with internal controls, or randomized controlled trials

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate guidance on the use of hormone replacement therapy for the prevention of cardiovascular and cerebrovascular disease

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Abramson BL. Postmenopausal hormone replacement therapy for primary prevention of cardiovascular and cerebrovascular disease. Recommendation statement from the Canadian Task Force on Preventive Health Care. CMAJ 2004 Apr 27;170(9):1388-9. [35 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Apr 27

GUIDELINE DEVELOPER(S)

Canadian Task Force on Preventive Health Care - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

The Canadian Task Force on Preventive Health Care (CTFPHC) is funded through a partnership between the Provincial and Territorial Ministries of Health and Health Canada.

GUIDELINE COMMITTEE

Canadian Task Force on Preventive Health Care (CTFPHC)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Competing interests: none declared

GUIDELINE STATUS

This is the current release of the guideline.

A complete list of planned reviews, updates and revisions is available under the What's New section at the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.

Print copies: Available from the Canadian Task Force on Preventive Health Care, 100 Collip Circle, Suite 117, London, Ontario, Canada, N6G 4X8.

AVAILABILITY OF COMPANION DOCUMENTS

- Abramson, BL with the Canadian Task Force on Preventive Health Care. Postmenopausal hormone replacement therapy for the primary prevention of cardiovascular and cerebrovascular disease. Systematic Review & Recommendations. CTFPHC Technical Report #03-2. March 2003. London, ON: Canadian Task Force. Available from the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.
- Abramson, BL. Postmenopausal hormone replacement therapy for primary prevention of cardiovascular and cerebrovascular disease. Recommendation table. Ottawa: Health Canada, 2003 Feb. Available from the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.
- Stachenko S. Preventive guidelines: their role in clinical prevention and health promotion. Ottawa: Health Canada, 1994. Available from the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.
- CTFPHC history/methodology. Ottawa: Health Canada, 1997. Available from the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.
- Quick tables of current recommendations. Ottawa: Health Canada, 1997. Available from the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 13, 2004. The information was verified by the guideline developer on September 15, 2004.

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